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S. H. Liu, … , C. W. Wang, K. P. Chang

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Research Article

CALCIUM AND PHOSPHORUS METABOLISM IN OSTEOMALACIA. V. THE EFFECT OF VARYING LEVELS AND RATIOS OF CALCIUM TO PHOSPHORUS INTAKE ON THEIR SERUM LEVELS, PATHS OF EXCRETION AND BALANCES, IN THE PRESENCE OF CONTINUOUS VITAMIN D THERAPY

By S. H. LIU, C. C. SU, S. K. CHOU, H. I. CHU, C. W. WANG AND K. P. CHANG

(*Department of Medicine, Peiping Union Medical College, Peiping, China*)

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Osteomalacia is a bone disease more commonly seen and with greater clinical implications in North China than elsewhere (1, 2, 3). The principal cause of the skeletal demineralization resides in vitamin D deficiency, a combination of its lack in the diet and exclusion of sunlight. By reason of such deficiency, calcium given by mouth fails to be absorbed. Poor intestinal absorption rather than excessive elimination is incriminated because it has been demonstrated by the studies of Hannon et al. (4) that the endogenous calcium metabolism in patients with osteomalacia on low intake is within normal limits and that calcium administered parenterally is largely retained. Under such circumstances while the endogenous destructive activity in the bones may not be excessive, the reparative process is very much interfered with through defective intestinal absorption so that skeletal decalcification inevitably ensues. The limited intake of calcium in common Chinese dietaries (5), and periods of mineral stress incident to pregnancy and lactation are some of the contributing factors that enter into the pathogenesis of osteomalacia.

Studies of the effect of vitamin D in the treatment of osteomalacia (4, 6) demonstrate the remarkable conserving action of vitamin D on calcium and phosphorus metabolism. As a result of its administration, intestinal absorption is promoted and endogenous elimination is decreased so that large quantities of calcium and phosphorus are available for deposition in the bones. The actual amount of calcium and phosphorus retained depends upon the level and ratio of intake of these elements. It has been shown in two patients with osteomalacia undergoing reparation initiated by vitamin D (7) that calcium retention varied directly with calcium intake while phosphorus retention was limited by both calcium and phosphorus intake. Fecal calcium likewise varied directly with calcium intake while fecal phosphorus was parallel with both calcium and phosphorus intake. When calcium supply is limited in relation to phosphorus (low Ca : P ratio) practically all the calcium absorbed is deposited, none appearing in the urine. On the other hand, when phosphorus supply is short compared with calcium (high Ca : P ratio), all the available phosphorus is retained and urinary phosphorus vanishes. Conservation of excretion through the urinary tract and efficient absorption through the intestinal canal account for the markedly positive balances in osteomalacia when reparation is brought about under the influence of vitamin D.

Similar observations on the effects of variations of the levels and ratios of calcium to phosphorus intake on their serum levels, paths of excretion and balances have been made on another patient with healing osteomalacia. But in contrast to the previous patients who received vitamin D only prior to the observations, the present subject was given vitamin D throughout the entire study so as to obviate any uncertainty in ascribing the metabolic results obtained to vitamin D action. Moreover, attempt was made in the present study to secure more nearly metabolic equilibrium by using three 4-day periods for each level or ratio of dietary intake. The data obtained from this patient, together with those from another subject having syphilitic osteitis of right radius and tibia without general metabolic disturbance, taken as a control, constitute the basis of discussion in the present communication.

PROCEDURE

The clinical histories of the two subjects are briefly described in the appendix. Subject 1, H. F. M., was a woman of 32 with advanced osteomalacia of seven years' duration. While skeletal rarefaction and deformities were marked, her serum calcium and phosphorus were within normal limits. She was placed on various diets, the compositions of which are given in Table I. All the diets were low in calcium but contained varying amounts of phosphorus. The desired high levels of calcium intake were attained by giving appropriate quantities of a saturated solution of calcium lactate (7.7 per cent). At a given level of calcium intake, the phosphorus level was progressively increased by giving Diets 5, 2, 3 and 4 in that order. There were altogether 3 levels of calcium and 4 levels of phosphorus intake, making a total of 12 different ratios. Three four-day periods were devoted to each ratio of calcium to phosphorus intake. The first five periods concerned preliminary observations without vitamin D, but after that 1 cc. of Vigantol, an oily solution of irradiated ergosterol containing 15,000 international units of vitamin D per cc., was given daily.

Subject 2, L. Y. H., was a man of 24 with syphilitic osteitis of right radius and tibia, the rest of the skeleton showing normal density and texture on x-ray examination. As localized bone involvement by infection usually does not give rise to general metabolic disturbances, the patient may be regarded as a control for the present purpose. He was given Diets 1, 2 and 3 in that sequence. With each diet, namely, with each level of phos-

TABLE I

Composition of diets in grams per day †

Articles of food	Vitamin D	Subject 1 (H. F. M.)						Subject 2 (L. Y. H.)		
		Diet 1	Diet 2	Diet 3	Diet 4	Diet 5a	Diet 5b	Diet 1	Diet 2	Diet 3
Millet	±	50		50	50					100
Rice	±		50						200	100
Glutinous rice						20	16		50	
Oatmeal	±				100					
White wheat flour	+	50	150	200	75	150	120	300	200	150
Mung bean flour						100	80			
Peanut	*				25					
Egg	+			30	30					
Egg white	±					300	240	300	100	
Pork	*	150	75	50	25				25	100
Chicken	*	100	50	50	75					100
Beef	±		50	75	75					
Aroid	*	50	50	50						100
Potato	*	50							50	50
Sweet potato	±				50					
Carrot	±				50					
Turnip	±		50	100		100	80			
Cabbage	±	100	100	150	100					100
Onion	*								50	
Chinese lettuce									100	
Spinach	±							100		
Apple	*	50	50	50						50
Banana	*					50	40			
Orange	*					50	40			
Lard								50	31	
Butter	++							30	20	
Sesame oil		32	45	50	50	70	56	40	20	50
Table salt		4	4	4	4	4	3.2	4	6	6
Sugar		21	20	20	24	50	40	60	24	
Soy bean sauce		5	5	5	5	5	4			
Protein		65	59	69	77	58	46	71	62	80
Carbohydrate		102	192	232	211	284	227	286	392	307
Fat		63	70	79	94	73	58	120	76	76
Calories		1235	1642	1923	2000	2022	1614	2508	2500	2232
Calcium		0.138	0.140	0.191	0.181	0.176	0.140	0.178	0.118	0.173
Phosphorus		0.914	0.627	0.925	1.163	0.324	0.259	0.402	0.582	1.094
Nitrogen		10.40	9.12	10.68	12.39	8.28	6.64	10.82	8.69	11.51

† Calcium, phosphorus and nitrogen values are actually determined, and vitamin D values taken from Wu (8); ++ good amount; + fair amount; ± no appreciable amount; * doubtful or undetermined. Approximate computation of the acid base balance of the diets according to Sherman (9) gives potential acidities ranging from 19 to 35 cc. of normal acid for Subject 1, and 30 to 44 cc. for Subject 2.

phorus intake, calcium was raised by the addition of desired amounts of calcium lactate. With this patient, 3 levels each of calcium and phosphorus were studied, giving 9 combinations. No vitamin D was administered.

Calculation of the acid base balance of the diets according to Sherman (9) showed that all the diets were potentially acid with relatively small variations, but the computation should be considered only approximate, because of the uncertainty of the applicability of Sherman's figures to local foodstuffs.

Stool and urine respectively of each period were pooled for analysis. Venepuncture was done before breakfast at the beginning of each period. Metabolic ward routine and analytical methods for calcium, phosphorus and nitrogen of food, urine, stool and blood were described previously (7).

RESULTS

Serum calcium and phosphorus. As seen from Figure 1, Subject 1 maintained a fairly stationary level of serum calcium throughout the period of 212 days of continuous observation, the range be-

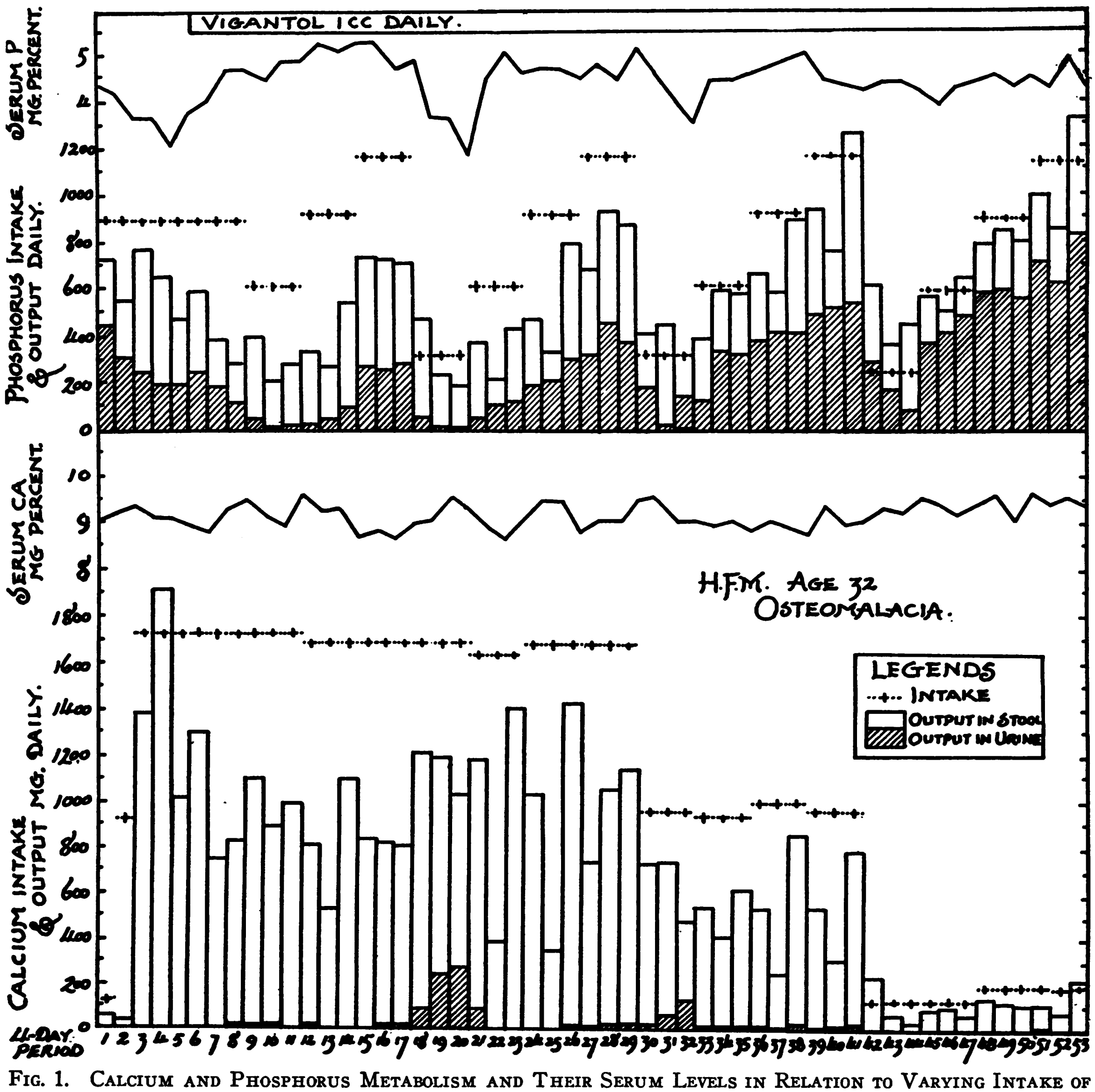

Fig. 1. Calcium and Phosphorus Metabolism and Their Serum Levels in Relation to Varying Intake of Calcium and Phosphorus in Subject 1

ing from 8.7 to 9.6 mgm. per 100 cc. and the trend bearing no apparent relation to the dietary changes. The serum inorganic phosphorus level, however, varied from 2.9 to 5.3, a difference of 2.4 mgm. per 100 cc. The phosphorus level, beginning at 4.3 mgm. per 100 cc., gradually went down to 3.0 as calcium intake in the diet was stepped up to 1.7 grams (Period 4). While the calcium intake was maintained at this high level, the phosphorus curve began to climb as vitamin D was given, and rose to a maximum of 5.3 as the phosphorus intake was progressively raised (Period 15). The phosphorus curve showed a second drop in Periods 18 to 20 when the phosphorus intake was suddenly decreased to a minimum, and a subsequent recovery to the high level in Periods 27 to 29 when high phosphorus intake was restored. When calcium intake was maintained at a lower level, namely, 1.0 gram as in Periods 30 to 41, similar changes in the phosphorus intake brought about a repetition of the cycle of events in the serum phosphorus curve, but to a lesser extent. But when the calcium intake was kept minimal (Periods 42 to 53), lowering of the phosphorus intake failed to elicit any significant change in serum phosphorus. In other words, serum phosphorus varied more with the ratio of calcium to phosphorus than with their actual levels in the intake. Whenever the ratio is high serum phosphorus drops.

In Subject 2 (Figure 2) the serum calcium level was also relatively constant, varying from a minimum of 9.0 to a maximum of 10.2 mgm. per 100 cc., irrespective of the calcium and phosphorus intake. The serum phosphorus, compared with that of Subject 1, showed much less fluctuation, ranging as it did between 3.9 and 5.1 mgm. per 100 cc. Moreover, the trend of variation with dietary intake seemed to be opposite in direction to that seen in Case 1. When the calcium supply was short in relation to phosphorus (low Ca:P ratio), the serum phosphorus tended to fall with a subsequent rise when calcium intake was stepwise increased. However, the changes observed were not sufficiently pronounced to render their significance indubitable.

From the above observations it may be concluded that dietary variations of calcium and phosphorus are not significantly reflected in the serum calcium level. This is true in osteomalacia, as

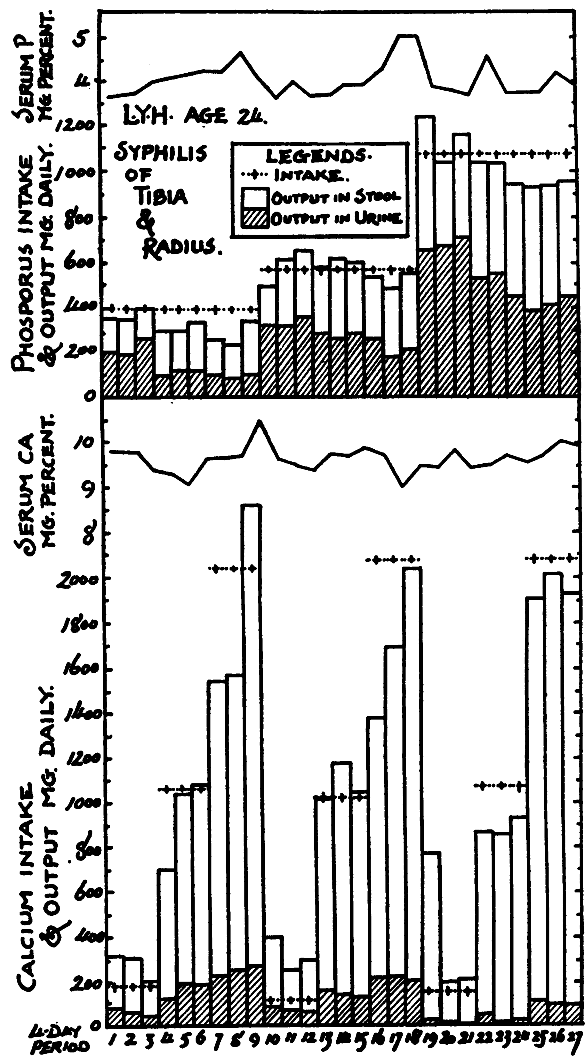

FIG. 2. CALCIUM AND PHOSPHORUS METABOLISM AND THEIR SERUM LEVELS IN RELATION TO VARYING INTAKE OF CALCIUM AND PHOSPHORUS IN SUBJECT 2

well as in the control case, probably on account of the protective influence of vitamin D, as in its absence the serum calcium and inorganic phosphorus reflect remarkably the ratio of these elements in the diet as shown by Shohl (10) in experimental rickets in rats. Dietary changes may cause fluctuations in serum phosphorus, however, even when vitamin D is added to the diet. In healing osteomalacia, for example, where there is marked deposition of calcium and phosphorus in the bones, a deficiency in intake of phosphorus relative to calcium intake results in a fall in serum phosphorus; and excess phosphorus intake relative to calcium intake may result in a rise in serum phosphorus. On the other hand, in the case of localized bone disease and presumably in normal individuals where excesses in supply are excreted and deficiencies in intake are made up from the large skeletal store, serum phosphorus level is less subject to fluctuation.

Paths of excretion. The data from Subject 1 as presented in Figure 1 and as averaged in Table II demonstrate a general reciprocal relationship between urinary calcium and phosphorus. At a constant level of calcium intake, progressive increment of phosphorus supply tended to decrease the urinary calcium sometimes to the point of disappearance, and at the same time to augment the urinary phosphorus.

If the results at the same level of dietary phosphorus are taken for comparison successive addition of calcium intake increased the urinary calcium coincident with a gradual and steady diminution of urinary phosphorus. In general, the magnitude of urinary excretion of calcium was small or negligible but it became considerable when calcium was supplied far in excess of the dietary phosphorus (Periods 18 to 20). Likewise, urinary excretion of phosphorus was very much limited on low phosphorus diet, but became dominant when phosphorus supply was far in excess of dietary calcium (Periods 51 to 53).

Fecal calcium increased consistently with the calcium intake, having little relation with the phosphorus supply, while fecal phosphorus was directly related not only with dietary phosphorus, but also with dietary calcium. Intestinal elimination of phosphorus, then, depends not only on its supply in the diet, but also on the amount of calcium presented in the intestine for excretion.

In Subject 2 (Figure 2 and Table III) similar results were obtained. The magnitude of urinary calcium excretion was greater, and it never disappeared, even when the supply was minimal in the presence of large phosphorus intake (Periods 19 to 21). Likewise, when phosphorus intake was minimal in the presence of excessive dietary calcium, urinary phosphorus, though decreased, was still considerable, compared with that in healing osteomalacia. The fecal elimination of calcium and, to a lesser degree, of phosphorus in Subject 2 was greater also, but the correlation between the intake of calcium and phosphorus and their output in the stool was just as close. In addition to the tendency for fecal phosphorus to vary directly with calcium intake, there was a

TABLE II

Subject 1. Average daily calcium and phosphorus metabolism

Period number	Diet number	Intake			Output					Balances				
		Ca	P	Ratio Ca : P	Urinary		Fecal			Ca	P	N_2	P corrected	Ratio Ca : P corrected
					Ca	P	Ca	P	Dry weight					
		mgm.	*mgm.*		*mgm.*	*mgm.*	*mgm.*	*mgm.*	*grams*	*mgm.*	*mgm.*	*grams*	*mgm.*	
3–5	1	1738	914	1.90	0	222	1444	420	19.4	294	272	1.05	212	1.39
*6–8	1	1738	914	1.90	5	190	956	238	12.7	777	486	1.43	404	1.93
9–11	2	1740	627	2.14	19	25	962	283	17.0	759	319	1.22	249	3.05
12–14	3	1691	925	1.83	7	62	822	328	17.9	862	535	2.24	406	2.12
15–17	4	1681	1163	1.45	6	297	829	438	22.8	846	428	2.40	287	2.94
18–20	5	1676	324	5.18	209	23	945	287	20.1	522	14	0.98	−44	
21–23	2	1640	627	2.60	31	85	970	261	18.9	639	281	0.71	239	2.67
24–26	3	1691	925	1.83	4	238	935	296	18.3	752	391	1.56	301	2.50
27–29	4	1681	1163	1.45	19	393	960	444	22.2	702	326	2.17	201	3.49
30–32	5	976	324	3.01	77	37	582	318	19.7	313	−31	1.59	−124	
33–35	2	940	627	1.50	6	252	545	249	15.9	389	126	0.22	113	3.44
36–38	3	994	924	1.08	8	413	535	301	16.5	451	210	2.17	82	5.50
39–41	4	981	1163	0.84	6	528	540	408	19.0	435	227	1.50	139	3.13
42–44	5*a*	141	259	0.54	3	184	111	299	18.4	27	−224	−0.01	−223	
45–47	2	140	627	0.22	4	436	78	157	11.6	58	34	0.70	−6	
48–50	3	194	924	0.21	1	593	129	242	18.3	64	89	1.40	7	
51–53	4	181	1163	0.16	4	744	137	335	20.2	40	84	1.11	20	2.00

* Vigantol 1 cc. daily started from this period and continued throughout.

TABLE III

Subject 2. Average daily calcium and phosphorus metabolism

Period number	Diet number	Intake			Output					Balances			
		Ca	P	Ratio Ca : P	Urinary		Fecal			Ca	P	N_2	P corrected
					Ca	P	Ca	P	Dry weight				
		mgm.	*mgm.*		*mgm.*	*mgm.*	*mgm.*	*mgm.*	*grams*	*mgm.*	*mgm.*	*mgm.*	*mgm.*
1– 3	1	178	402	0.44	73	232	207	153	20.3	−102	28	1.65	−69
4– 6	1	1058	402	2.63	189	158	736	155	20.5	133	89	2.27	−45
7– 9	1	2043	402	5.08	252	104	1561	183	18.2	230	115	2.33	−22
10–12	2	118	582	0.20	79	341	241	255	16.5	−202	−14	1.16	−82
13–15	2	1023	582	1.76	153	282	928	323	21.4	58	−23	1.09	−87
16–18	2	2080	582	3.58	211	221	1495	319	21.2	374	42	1.16	−26
19–21	3	173	1094	0.16	19	695	373	471	21.0	−219	−72	0.60	−107
22–24	3	1078	1094	0.99	36	519	859	492	20.7	183	83	0.50	54
25–27	3	2084	1094	1.91	116	414	1812	525	25.4	156	155	0.48	127

discernible but slight tendency for the fecal calcium to vary directly with phosphorus intake.

As the average daily dry fecal weights in both cases varied only slightly on the various diets, it is unlikely that variations in roughage were sufficiently large to play an important rôle in the intestinal elimination of calcium and phosphorus.

Balances. While calcium balance may be taken to represent the state of bone metabolism, phosphorus balance is under the dual influence of bone and soft tissue metabolism. For every 17 grams of nitrogen retained or lost, 1 gram of phosphorus is retained or lost. To calculate the amount of phosphorus actually involved with calcium in bone metabolism, the total phosphorus balance is corrected by an amount equivalent to nitrogen balance. The corrected phosphorus balances are set forth in Tables II and III. In Table II it may be of interest to note the remarkable effect of vitamin D on calcium balance in osteomalacia. Prior to vitamin D administration the patient retained 294 mgm. of calcium on an intake of 1738 mgm. per day (Periods 3 to 5), but after its administration the retention increased to 777 mgm. on the same intake (Periods 6 to 8), the improvement being mainly due to lessened elimination in the stool.

To facilitate comparison, Tables IV and V are constructed in which calcium and corrected phosphorus balances are grouped according to intake. Subject 1 (as seen in the upper part of Table IV) exhibited a striking dependence of calcium balance on calcium intake. Calcium retention on the average increased steadily from 47 to 654 mgm. per day as calcium intake was progressively raised from 164 to 1672 mgm. per day, regardless of phosphorus intake. On the other hand, at a given

TABLE IV

Subject 1. The effect of calcium and phosphorus intake on their balances

Calcium intake		Calcium balance at the phosphorus intake of				Average Ca balance at same Ca intake regardless of P intake
Range	Level	324 mgm.	627 mgm.	922 mgm.	1163 mgm.	
mgm.	*mgm.*	*mgm.*	*mgm.*	*mgm.*	*mgm.*	*mgm.*
140–194	164	*0.52** 27	*0.22* 58	*0.21* 64	*0.16* 40	47
940–994	973	*3.01* 313	*1.50* 389	*1.08* 451	*0.84* 435	397
1640–1691	1672	*5.18* 522	*2.60* 639	*1.83* 752	*1.45* 702	654
Average of Ca balance at same P intake regardless of Ca intake		287	362	422	392	
Calcium intake		Phosphorus balance at the phosphorus intake of				Average P balance at same Ca intake regardless of P intake
Range	Level	324 mgm.	627 mgm.	922 mgm.	1163 mgm.	
140–194	164	*0.52* −223	*0.22* −6	*0.21* 7	*0.16* 20	−50
940–994	973	*3.01* −124	*1.50* 113	*1.08* 82	*0.84* 139	52
1640–1691	1672	*5.18* −44	*2.60* 239	*1.83* 301	*1.45* 201	174
Average P balance at same P intake regardless of Ca intake		−130	115	130	120	

* Figures in italics are ratios of calcium to phosphorus intake.

level of calcium intake, progressive increment of dietary phosphorus up to 922 mgm. per day resulted in a slight ascending tendency in the calcium balance, but further increase to 1163 mgm. failed to improve the calcium balance which, in fact, fell somewhat at the latter level of phosphorus intake. Corrected phosphorus balance likewise depended more on calcium than on phosphorus intake. When calcium intake was raised from 164 to 1672 mgm., the average phosphorus balance increased from − 50 to + 174 mgm.; whereas various levels of phosphorus intake made no striking difference to the phosphorus balance except in the case of minimal phosphorus intake where negative balance prevailed.

Balance data on Subject 2, summarized in Table V, show essentially the same findings, namely, the greater importance of calcium as the limiting factor in both calcium and phosphorus balances. However, on a minimal calcium intake of 145 mgm. he lost on the average 174 mgm. per day in contrast to Subject 1 who gained 47 mgm. on an intake of 164 mgm. The degree of calcium loss on a minimal intake in Subject 2 was within normal limits (11), while the behavior of Subject 1 was usually conservative. Thus the latter stored approximately 95 grams of calcium and 43 grams of phosphorus in the period of 200 days, equivalent to 15 per cent of the stores which should be in the body, in contrast to the control patient who retained only 5.9 grams of calcium and 4.8 grams of phosphorus in 108 days.

TABLE V

Subject 2. The effect of calcium and phosphorus intake on their balances

Calcium intake		Calcium balance at the phosphorus intake of			Average Ca balance at same Ca intake regardless of P intake
Range	Level	402 mgm.	582 mgm.	1094 mgm.	
mgm.	*mgm.*	*mgm.*	*mgm.*	*mgm.*	*mgm.*
112–178	145	*0.44** −102	*0.20* −202	*0.16* −219	−174
1012–1078	1040	*2.63* 113	*1.76* −58	*0.99* 183	86
2012–2084	2055	*5.08* 230	*3.58* 374	*1.91* 156	253
Average Ca balance at same P intake regardless of Ca intake		87	38	40	

Calcium intake		Phosphorus balance at the phosphorus intake of			Average P balance at same Ca intake regardless of P intake
Range	Level	402 mgm.	582 mgm.	1094 mgm.	
112–178	145	*0.44* −69	*0.20* −82	*0.16* −107	−86
1012–1078	1040	*2.63* −45	*1.76* −87	*0.99* 54	−26
2012–2084	2055	*5.08* −22	*3.58* −26	*1.91* 126	26
Average P balance at same P intake regardless of Ca intake		−45	−65	24	

* Figures in italics are ratios of calcium to phosphorus intake.

Examination of the ratios of calcium to corrected phosphorus balance (Table II) shows that they are above 2 in the majority of instances, and above 3 in several instances, bearing no close relationship with the ratios of intake. If we accept the mineral composition of normal bone as $CaCO_3 . 2Ca_3(PO_4)_2$ according to the x-ray analysis of Roseberry, Hastings and Morse (12), then the ratio of Ca : P should be 2.26. The fact that the ratios of retention in Subject 1 were usually higher than that prescribed for normal bone would suggest that more calcium was deposited as $CaCO_3$ than $Ca_3(PO_4)_2$ in the new bone formation or that calcium suffered to a greater extent than phosphorus during the prior demineralization. As to the actual amount of calcium retained, the maximum was 752 mgm. (or 45 per cent of intake) on an intake of 1672 mgm. calcium and 922 mgm. phosphorus giving a ratio of 1.83 (Table IV). This happens to be also the level and ratio of intake associated with the largest retention of phosphorus, namely, 301 mgm. (or 32 per cent of intake). Thus both calcium and phosphorus have to be given at fairly high levels with a ratio approaching 2 in order to secure maximal retention of both elements. Otherwise, the ratio made very little difference to the calcium balance which depended mainly on the level of intake, in conformity with the work of Shohl (10).

DISCUSSION

The present results obtained with the patient with osteomalacia receiving continuous administration of vitamin D are in entire agreement with those of previous studies on patients whose treatment with vitamin D was discontinued after relatively short periods of 4 to 6 weeks when its maximum effect had been attained. The behavior of serum calcium and phosphorus, the manner of conservation of these elements through the urinary and intestinal tracts, the ability of the patients to maintain positive calcium balance on minimal intake and to retain large amounts of it on higher levels of intake, and finally the relatively greater importance of calcium intake rather than phosphorus intake as the limiting factor in both calcium and phosphorus retention are essentially the same in both instances. Thus vitamin D, once given to the extent of its maximum effect, will maintain its action unabated for at least several months after its discontinuation, and its continuous administration in the treatment of osteomalacia does not seem to offer any substantial advantage.

In the therapy of osteomalacia, while vitamin D administration corrects the basic metabolic defect, it is essential that both calcium and phosphorus be given at fairly high levels, preferably with a ratio of approximately 2 in order to promote large retention of both elements and therefore rapid restoration of the mineral contents of the depleted osseous system. With ordinary Chinese dietaries which are low in calcium and fairly high in phosphorus, the desired high level of calcium intake has to be supplied as calcium salts, while that of phosphorus intake can easily be taken care of by the diet.

The behavior of the patient without skeletal decalcification resembles that of patients having healing osteomalacia in respect to the reciprocal relationship between urinary calcium and phosphorus, the approximately parallel relationship between stool calcium and phosphorus, the dependence of both calcium and phosphorus balances on calcium intake, and the slight effect of phosphorus intake as a limiting factor in both calcium and phosphorus retention. On the other hand, he differs in that the serum phosphorus is relatively more stable toward dietary changes, and in that the magnitudes of urinary and stool excretion of calcium and phosphorus are greater, resulting in negative balance on low intake and only slight retention on higher levels of intake. These differences are but an expression of the fact that in a relatively normal individual measures of mineral conservation are less urgently in need of application.

SUMMARY

1. In two patients, one with osteomalacia under reparation and the other with syphilitic osteitis of radius and tibia, the serum levels of calcium and phosphorus, paths of excretion and retention of these elements were studied in relation to their levels and ratios of intake.

2. Serum calcium was fairly constant in both cases, while serum inorganic phosphorus tended to lower with a higher ratio of Ca : P intake in the first patient. No such variations were demonstrable in the second patient.

3. A reciprocal relationship between calcium and phosphorus in urine was shown in both instances. Whenever the Ca : P ratio in the diet was high, urinary calcium increased, while urinary phosphorus diminished. An opposite change in the ratio resulted in a diminution of urinary calcium coinciding with a rise of urinary phosphorus.

4. Fecal calcium and phosphorus varied with their respective level of intake, while fecal phosphorus was also partly dependent on calcium intake.

5. Retention of either calcium or phosphorus depended more on the calcium than phosphorus intake, although both had to be supplied in fairly large quantities with a Ca : P ratio of approximately 2 in order to realize maximal retention of both elements to promote efficient repair of skeletal demineralization in osteomalacia.

6. The present study with prolonged administration of vitamin D revealed no essential difference from the previous work with limited vitamin D therapy, showing that the effect of vitamin D lasts long after its discontinuation.

CASE HISTORIES

Case 1. H. F. M., a Chinese housewife of 32, was admitted on August 28, 1935 for pain in back and legs and difficulty in walking. These began 7 years prior to admission when she had her first pregnancy. Labor was spontaneous but lasted for more than 24 hours. After that she had periodical exacerbations of the above symptoms in winter and spring when she kept herself indoors. The second pregnancy occurred 4 years after the first and resulted in a seven months' premature labor lasting more than 48 hours. Henceforth symptoms became worse. She could neither stand on her feet nor walk without support. Her diet had always been extremely poor. In the cold months she lived on cereals and salted vegetables. In the warmer months some fresh vegetables were available. Meat was seldom taken and eggs only occasionally.

Examination on admission confirmed her statement about her inability to stand or walk without support. Body weight was 40 kgm. and height 136 cm. On lying down, the right thigh was slightly flexed and abducted, with the knee joint held in 30° flexion. Movement at the hip joint caused pain. There was no tenderness along the lower extremities. The pelvis was of the funnel type. Symphysis pubis protruded and sacrum was prominent. Tenderness was marked over the sacro-iliac joints, pelvic bones, lower ribs and lumbar vertebrae. The right upper molar teeth and lower incisors were loose. Other physical findings were normal. X-ray showed a deformed pelvis and general osteoporosis and some pleural thickening with adhesions in the right lower chest. Blood calcium was 8.92, phosphorus 3.29 mgm. per cent, and plasma phosphatase 4.9 units (Bodansky). Blood counts and urinalysis were essentially normal. Stool was positive for ova of ascaris. Metabolic studies were carried out in four-day periods for 212 days from October 4, 1935 to May 2, 1936. Besides the dietary treatment and vitamin D administration she also received physiotherapy in the form of exercises for extension of the hip and spine and infra-red irradiation. At the time of discharge she could walk fairly well without support, and x-ray of bones revealed definitely increased density.

Case 2. L. Y. S., a Chinese man of 24, entered on July 13, 1934 for swelling and lengthening of the right leg of 8 years' duration and of the right forearm of two years' duration. Onset was insidious without history of injury. He had occasional low grade fever and pain after prolonged walking. He had had venereal exposures.

The patient was found to be slightly undernourished. Body weight was 42.2 kgm. and height 159 cm. His right leg was 5.5 cm. longer than the left and also bigger especially in the lower part. There was slight tenderness over the right tibia, and the overlying skin was slightly warmer than that of the left side. The knee and ankle were not involved. Right forearm was 1.5 cm. longer than the left. The elbow and wrist were free. Other physical findings were essentially normal. X-ray of the bones showed irregular areas of condensation and rarefaction in the cortex involving the entire length of right tibia and radius. The rest of the skeleton appeared normal. Blood and urine examinations revealed no significant findings. Stools contained ova of ascaris. Blood calcium was 9.7 and phosphorus 4.2 mgm. per cent. Basal metabolic rate was + 8.4 per cent. Blood Wassermann and Kahn tests were strongly positive. Metabolic studies were carried on for 108 days (27 four-day periods from September 18, 1934 to January 3, 1935). Subsequent intensive antisyphilitic treatment to date has given rise to marked improvement in the bone lesions.

BIBLIOGRAPHY

1. Maxwell, J. P., Osteomalacia in China. China M. J., 1923, **37**, 625.
2. Maxwell, J. P., Further studies in osteomalacia. Proc. Roy. Soc. Med. (Section Obst. and Gynec.), 1930, **23**, 19.
3. Maxwell, J. P., and Miles, L. M., Osteomalacia in China. J. Obst. and Gynec. Brit. Emp., 1925, **32**, 433.
4. Hannon, R. R., Liu, S. H., Chu, H. I., Wang, S. H., Chen, K. C., and Chou, S. K., Calcium and phosphorus metabolism in osteomalacia. I. The effect of vitamin D and its apparent duration. Chinese Med. J., 1934, **48**, 623.
5. Wu, H., and Wu, D. Y., Dietaries of Peking. Chinese J. Physiol. (Report Series), 1928, **1**, 135.
6. Liu, S. H., Hannon, R. R., Chu, H. I., Chen, K. C., Chou, S. K., and Wang, S. H., Calcium and phosphorus metabolism in osteomalacia. II. Further studies on the response to vitamin D of patients with osteomalacia. Chinese Med. J., 1935, **49**, 1.
7. Liu, S. H., Hannon, R. R., Chou, S. K., Chen, K. C., Chu, H. I., and Wang, S. H., Calcium and phosphorus metabolism in osteomalacia. III. The effects of varying levels and ratios of intake of calcium to phosphorus on their serum levels, paths of excretion and balances. Chinese J. Physiol., 1935, **9**, 101.
8. Wu, H., Nutritive value of Chinese foods. Chinese J. Physiol. (Report Series), 1928, **1**, 153.
9. Sherman, H. C., Chemistry of Food and Nutrition. Macmillan Co., New York, 1928, 3d ed.
10. Shohl, A. T., Rickets in rats. XV. The effect of low calcium-high phosphorus diets at various levels and ratios upon the production of rickets and tetany. J. Nutrition, 1936, **11**, 275.
11. Bauer, W., Albright, F., and Aub, J. C., Studies of calcium and phosphorus metabolism. II. The calcium excretion of normal individuals on a low calcium diet, also data on a case of pregnancy. J. Clin. Invest., 1929, **7**, 75.
12. Roseberry, H. H., Hastings, A. B., and Morse, J. K., X-ray analysis of bone and teeth. J. Biol. Chem., 1931, **90**, 395.